Original Article

The Study of Aortic Stiffness in Different Hypertension Subtypes in Dialysis Patients

Li-Tao CHENG[1),2)], Hui-Min CHEN[1),3)], Li-Jun TANG[1),4)], Wen TANG[1)],
Hai-Yan HUANG[2)], Yue GU[1)], and Tao WANG[1),2)]

The aim of this study was to validate whether differences in aortic stiffness are responsible for the differences in cardiovascular mortality among hypertension subtypes. Twenty hundred and fifty continuous ambulatory peritoneal dialysis patients were included in the present study. They were classified into four groups: normotensives (*n*=92) with systolic blood pressure (SBP) <140 mmHg and diastolic blood pressure (DBP) <90 mmHg; isolated systolic hypertensives (ISH, *n*=84) with SBP ≥140 mmHg and DBP <90 mmHg; isolated diastolic hypertensives (IDH, *n*=21) with SBP <140 mmHg and DBP ≥90 mmHg; and systolic-diastolic hypertensives (SDH, *n*=53) with SBP ≥140 mmHg and DBP ≥90 mmHg. Aortic stiffness was assessed by pulse pressure, central pressure parameters and pulse wave velocity. The IDH group had more male patients and a lower mean age than the other groups. The percentage of diabetes in the ISH group was higher than that in the other groups. The comparisons of aortic stiffness showed that the ISH and SDH groups had higher aortic stiffness than the normotension and IDH groups. The aortic stiffness in the ISH group was also higher than that in the SDH group, but there was no significant difference in aortic stiffness between the normotension and IDH groups. In conclusion, this study showed that aortic stiffness was significantly different among different hypertension subtypes, which might be an underlying cause of the differences in cardiovascular mortality among the hypertension subtypes. (*Hypertens Res* 2008; 31: 593–599)

***Key Words*: hypertension, isolated diastolic hypertension, aortic stiffness, pulse wave velocity, peritoneal dialysis**

Introduction

Hypertension is usually diagnosed as an elevation of both systolic and diastolic blood pressure (SBP and DBP, respectively) (*1*). However, it is not uncommon to see clinical cases in which only the SBP or only the DBP criterion is met. Such patients are considered to have isolated systolic hypertension (ISH) or isolated diastolic hypertension (IDH), which are noticeably distinct from the traditional systolic-diastolic hypertension (SDH) (*1*). Previous studies have shown that the prevalence of these hypertension subtypes is dramatically different in different age populations. According to the Third National Health and Nutrition Examination Survey (NHANES III, 1988 to 1991) (*2*), IDH is the most frequent form of hypertension in young adults <40 years old while IDH and SDH are equally prevalent in those aged 40 to 49 years. In contrast, ISH is the dominant form of hypertension from the sixth decade of life and beyond (*2*, *3*).

However, it is even more interesting to note that different hypertension subtypes seem to have different risk for cardiovascular events, and thus different prognoses. Previous stud-

From the [1)]Division of Nephrology, Peking University Third Hospital, Beijing, P.R. China; [2)]Division of Nephrology, Peking University First Hospital, Beijing, P.R. China; [3)]Division of Cardiology, the Second Clinical College of the Guangzhou University of Chinese Traditional Medicine, Guangzhou, P.R. China; and [4)]Division of Nephrology, Qilu Hospital of Shandong University, Ji'nan, P.R. China.
This study was supported by a grant from the Cheung Kong Scholar Programme, Ministry of Education, People's Republic of China (36-1).
Address for Reprints: Tao Wang, M.D., Ph.D., Division of Nephrology, Peking University Third Hospital, 49 North Garden Rd, Haidian District, Beijing 100083, P.R. China. E-mail: wangt@bjmu.edu.cn
Received April 16, 2007; Accepted in revised form October 10, 2007.

ies have shown that ISH is associated with an increased risk of cardiovascular morbidity and mortality as compared with SDH (*4–6*). In the case of IDH, the limited number of studies tends to suggest that this specific subtype is characterized with lower risk of cardiovascular mortality than ISH and SDH (*7–10*). Among these studies, one performed in Japan found that the risk of cardiovascular mortality in IDH patients is even lower than that in normotensive subjects (*9*).

The underlying mechanisms responsible for the differences in cardiovascular mortality among hypertension subtypes remain speculative. Although ISH is known to be a manifestation of increased aortic stiffness (*11–13*), it is still not clear whether other subtypes of hypertension, especially IDH, are associated with higher aortic stiffness as compared with normotension. To date, there has been no systematic study of the difference of aortic stiffness among different hypertension subtypes. In the present study, we employed a series of indices of aortic stiffness and tried to address this question in a group of continuous ambulatory peritoneal dialysis (CAPD) patients.

Methods

Study Population

CAPD patients were enrolled from our Peritoneal Dialysis Center. The exclusion criteria were: 1) dialysis duration of less than 3 months; 2) manifestation of congestive heart failure; and 3) hypotension (defined as SBP <90 mmHg and/or DBP <60 mmHg). Based on these criteria, 250 of the total of 314 patients registered in our center at that time were considered to be eligible for the present study. Written informed consent was obtained from every patient, and the ethics committee of Peking University approved the study protocol.

Measurement of Brachial Blood Pressure

To ensure the accuracy of measurements, a dedicated renal nurse was placed in charge of all blood pressure (BP) measurements; the nurse performed the measurements according to strict instructions but was not aware of the study protocol or objective. The mercury sphygmomanometer used was calibrated regularly. BP was measured in the morning (at between 7:45 and 10 AM) during the study months (from June to July, 2006). The patients were asked to take their usual antihypertensive medications, and were apprised of the potentially dangerous outcome of abruptly withdrawing these medications. However, they were asked not to take breakfast, since fasting plasma was to be taken for biochemical examination. All measurements were performed in a quiet room. Brachial BP was measured twice in a sitting position after patients had rested more than 10 min. If the patient's right arm had an arteriovenous fistula, BP measurement was carried out in the contralateral arm. Phase I and V of the Korotkoff sounds were taken respectively as SBP and DBP. Both SBP and DBP were taken as the average of two measurements. Brachial pulse pressure (PP) was calculated as SBP minus DBP.

Table 1. Demographic Characteristics of the Study Population

Number of patients	250
Male/female	109/141
Age, years	60±13
Weight, kg	61±11
Height, cm	160±8
Body mass index, kg/m^2	24±4
Dialysis duration, months	24±19
Etiology of uremia, %	
Chronic glomerulonephritis	31
Hypertension	24
Diabetes	20
Tubulo-interstitial nephritis	16
Unknown	9

Classification of the Subtypes of Hypertension

According to their brachial BP levels, these patients were classified into four subtypes: 1) normotensives (*1*): SBP <140 mmHg and DBP <90 mmHg; 2) isolated systolic hypertensives (ISH) (*1*): SBP ≥140 mmHg and DBP <90 mmHg; 3) isolated diastolic hypertensives (IDH) (*14*): SBP <140 mmHg and DBP ≥90 mmHg; and 4) systolic-diastolic hypertensives (SDH) (*1*): SBP ≥140 mmHg and DBP ≥90 mmHg.

Measurement of Central Pressure Parameters

The measurement of central pressure parameters was performed by radial applanation tonometry. The radial pressure waveform was measured by a Millar piezoresistive pressure transducer (SPC-301; Millar Instruments, Houston, USA) connected to an arterial waveform analysis device (SphygmoCor v7; AtCor Medical, Sydney, Australia). The aortic waveform was simulated and calculated out through a validated mathematical transfer function (SphygmoCor software system) to determine the central augmentation pressure (AP) and central pulse pressure (C-PP) (*15*, *16*). The augmentation index (AIx) was then calculated as AP divided by C-PP. The mean value of three consecutive measurements was taken for each subject. All measurements were performed by the same investigator (H.-Y. H.) to avoid inter-observer error. The intra-observer coefficient of variation (CV) was about 5% for AIx (range: 1.6 to 7.8%). All patients received this measurement.

Measurement of Pulse Wave Velocity

The carotid-femoral pulse wave velocity (PWV) measure-

Table 2. Comparison of Demographic Characteristics among the Different Hypertensive Subtypes

	Normotension	ISH	IDH	SDH
No. of patients	92	84	21	53
Percentage, %	37	34	8	21
Male/female[#]	34/58	35/49	15/6	25/28
Age, years	64±12[♭,z]	63±11	48±14[‡]	52±13[‡]
Weight, kg	60±10[x]	62±11	66±9	62±13
Height, cm	159±8[y]	160±8	165±6[†]	162±8
BMI, kg/m^2	24±3	24±4	24±4	24±4
PD duration, months	25±17	28±23	20±14	20±12*
Diabetes, %[#]	23.9	44.0	14.3	17.0
SBP, mmHg	122±11[‡,♭]	154±18[¶]	127±6[‡,♭]	159±14
DBP, mmHg	71±9[‡,♭,z]	76±7	92±3[‡,§]	98±6[‡]
AHM, %[#]	61	80	62	81
BUN, mmol/L	21±5[¶]	22±6	23±5	23±6
Creatinine, μmol/L	743±249[¶]	757±243	790±264	854±314*
Albumin, g/L	37±4[y]	37±3	40±4[†,§]	37±3
TCHO, mmol/L	5.5±1.4	5.3±0.9	5.2±1.0	5.1±1.2
pKt/V	1.3±0.5	1.3±0.4	1.2±0.4	1.2±0.4
rKt/V	0.5±0.6	0.4±0.5	0.7±0.7	0.5±0.6
tKt/V	1.8±0.5	1.8±0.4	1.8±0.5	1.8±0.6

ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; SDH, systolic-diastolic hypertension; BMI, body mass index; PD, peritoneal dialysis; SBP, systolic blood pressure; DBP, diastolic blood pressure; AHM, antihypertensive medication; BUN, blood nitrogen urea; TCHO, total cholesterol; pKt/V, peritoneal Kt/V; rKt/V, renal Kt/V; tKt/V; total Kt/V (rKt/V+pKt/V). Compared with ISH: *$p<0.05$; [†]$p<0.01$; [‡]$p<0.001$. Compared with SDH: [¶]$p<0.05$; [§]$p<0.01$; [♭]$p<0.001$. Compared with IDH: [x]$p<0.05$; [y]$p<0.01$; [z]$p<0.001$. [#]$p<0.05$ by χ^2 test.

ments were performed in all patients. The aortic PWV was determined using an automatic device, the Complior (Colson, Garges les Gonesses, France) (*17*), which allowed on-line pulse wave recording and automatic calculation of PWV. The common carotid artery and femoral artery pressure wave forms were recorded non-invasively using a TY-306 Fukuda pressure sensitive transducer (Fukuda, Tokyo, Japan). Measurement was repeated over 10 different cardiac cycles, and the mean value was used for the final analysis. The distance traveled by the pulse wave was measured over the body surface as the distance between the two recording sites (D), while the pulse transit time (t) was automatically determined by the Complior. PWV was automatically calculated as $PWV = D/t$. The details of this automatic method, as well as its validation and reproducibility, have been reported previously (*17*). All the PWV measurements were performed by one doctor (L.-J. T.) and the intra-observer CV ranged from 1.74% to 7.95%.

Statistical Analysis

Continuous variables were expressed as the means±SD while categorical variables were expressed as percentages or ratios. The comparison of continuous variables among different hypertension subgroups was performed by using ANOVA (for post hoc analysis, SNK was performed if equal variance was assumed and Tamhane's T2 test was performed if equal variance was not assumed). To control the confounding effect of age, gender, diabetic status and dialysis duration on PWV, the comparison of PWV among the four hypertension subtypes was performed with covariate analysis by treating these confounding factors as covariates. The comparison of categorical variables among different hypertension subtypes was performed by using the χ^2 test. All tests were two-sided. A value of $p<0.05$ was taken as statistically significant. All analysis was completed with SPSS software, version 11.0 (SPSS, Chicago, USA).

Results

Demographic Characteristic of the Study Population

The demographic characteristic of the study population are shown in Table 1. Among the 250 patients studied, 109 were males and 141 were females. The mean age was 60±13 years. The mean body mass index (BMI) was 24±4 kg/m^2. The mean dialysis duration was 24±19 months. The etiologies for uremia were: chronic glomerulonephritis (31.2%), hypertension (24.0%), diabetes (20.0%), tubulo-interstitial nephritis (16.0%) and unknown (11.2%).

Table 3. Comparison of Brachial PP and Simulated Central Pressure Parameters among the Different Hypertension Subtypes

	Normotension	ISH	IDH	SDH
PP, mmHg	51±12[‡,b,z]	78±20	35±6[‡,b]	61±14[‡]
AP, mmHg	11±6[‡,¶,y]	19±9	7±3[‡,b]	15±7[†]
C-PP, mmHg	39±12[‡,b,z]	63±17	27±6[‡,b]	48±13[‡]
AIx, %	25.8±9.6	27.0±8.3	24.7±6.3	28.4±8.3

ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; SDH, systolic-diastolic hypertension; PP, pulse pressure; AP, augmentation pressure; C-PP, central pulse pressure; AIx, augmentation index. Compared with ISH: †$p<0.01$; ‡$p<0.001$. Compared with SDH: ¶$p<0.05$; b$p<0.001$. Compared with IDH: y$p<0.01$; z$p<0.001$.

Comparisons of Demographic Characteristic and Biochemical Variables among Different Hypertension Subtypes

The comparisons of demographic characteristic and biochemical variables among different hypertension subtypes are shown in Table 2. There were 92, 84, 21 and 53 patients in the normotension, ISH, IDH and SDH subtype groups, respectively. The distribution of hypertension subtypes was as follows: normotension (37%), ISH (34%), IDH (8%) and SDH (21%). The gender distribution, weight and BMI among the normotension, ISH and SDH groups were not significantly different. However, the IDH group had a larger proportion of male patients as compared with the other subgroups ($p<0.05$). In addition, patients in the IDH group were the youngest among the four subtypes, while normotensive patients were significantly older than those in the IDH and SDH groups ($p<0.001$). The weight was comparable among the four groups, except that the weight in the normotension group was significantly lower than that of the IDH group ($p<0.001$). The body heights in the normotension and ISH groups were significantly lower than that of the IDH group ($p<0.01$), while the difference of height among the other groups was not significant. The dialysis duration among the four groups was comparable, except that it was significantly shorter in the SDH group than in the ISH group. Compared with the ISH group, the proportions of diabetes in the other three groups were significantly lower ($p<0.05$). Compared with the ISH and SDH groups, the normotension and IDH groups had significantly lower SBP ($p<0.001$). The SBP in the ISH group was also lower than that in SDH group, but there was no significant difference in SBP between the normotension and IDH groups. The DBP values in the IDH and SDH groups were significantly higher than those in the normotension and ISH groups ($p<0.001$), respectively. In addition, the DBP in the ISH group was also higher than that in the normotension group ($p<0.001$). The proportion of patients under antihypertensive medication was significantly different among the four groups ($p<0.05$), and this proportion in the normotension and IDH groups was lower than that in the ISH and SDH groups. Blood urea was comparable among the four groups except that it was significantly lower in the normotension group as compared to the SDH group ($p<0.05$). The creatinine in the SDH group was significantly higher as compared to the normotension and ISH groups ($p<0.05$), but the difference of creatinine among the other groups was not significant. The serum albumin in the IDH group was significantly higher than that in the other three groups ($p<0.01$), while albumin was not significantly different among the normotension, ISH and SDH groups. No significant difference in total cholesterol or the indices of dialysis adequacy (renal Kt/V [rKt/V], peritoneal Kt/V [pKt/V] and total Kt/V [tKt/V]) was observed among the four subgroups.

Comparisons of Brachial PP and Simulated Central Pressure Parameters among Different Hypertension Subtypes

The results of the comparisons of brachial PP and simulated central pressure parameters among the different hypertension subtypes are shown in Table 3. The ISH and IDH had the highest and lowest brachial PP among the four hypertension subtypes, and all comparisons between any two groups were statistically significant ($p<0.001$). The simulated central AP and C-PP showed a pattern of difference similar to that for brachial PP. However, there was no significant difference in AIx among the four hypertension subgroups.

Comparison of PWV among the Different Hypertension Subtypes

The results of the comparison of PWV among the different hypertension subtypes are shown in Fig. 1. The ISH and IDH groups had the highest (13.7±2.0 m/s) and lowest PWV (10.3±1.8 m/s) among the four hypertension subgroups (Fig. 1). The PWV values in the normotension and SDH groups were 10.4±1.6 m/s and 11.9±3.0 m/s, respectively. The PWV values in the normotension and IDH groups were significantly lower than those in the ISH and SDH groups ($p<0.05$). Compared with the SDH group, the ISH group also had higher PWV ($p<0.05$), while the difference in PWV between the normotension and IDH groups was not significantly different.

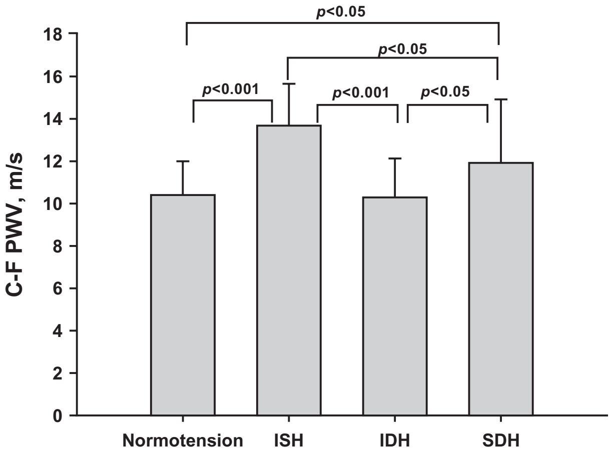

Fig. 1. *Comparison of carotid-femoral pulse wave velocity (C-F PWV) among the different hypertensive subtypes. ISH, isolated systolic hypertension; IDH, isolated diastolic hypertension; SDH, systolic-diastolic hypertension.*

Discussion

The major discovery in the present study was that the aortic stiffness was significantly different among different hypertension subtypes: ISH and SDH patients had higher aortic stiffness than normotensive and IDH patients, and ISH patients also had higher aortic stiffness than patients in the SDH group, while there was no significant difference in aortic stiffness between the normotensive and IDH groups. To our knowledge, this is the first study to systemically evaluate the difference of aortic stiffness among the different hypertension subtypes.

Indices to Assess Aortic Stiffness

This study employed a series of indices (brachial PP, simulated central pressure parameter and PWV) to assess aortic stiffness in the study population (Table 3 and Fig. 1). In recent years, brachial PP has been increasingly recognized as a surrogate of aortic stiffness because it increases with advancing age (*18*, *19*). Using brachial PP as the index of aortic stiffness, this study showed that the ranks of aortic stiffness from high to low were ISH, SDH, normotension and IDH. However, brachial PP is also under the influence of factors other than aortic stiffness, such as heart rate, cardiac contractility, venous pressure and the amplification phenomenon (*20*, *21*), which determines that brachial PP is not an ideal index of aortic stiffness. We therefore employed other indices—central pressure parameters to assess aortic stiffness. Theoretically, central pressure parameters are the direct measurements of aortic stiffness. The pressure wave generated by left ventricular ejection travels from the aorta to the periphery and reaches the peripheral reflection site, then travels back to the heart. As the aorta becomes stiffer, such as seen in the process of aging, the pressure wave travels faster and returns to the heart earlier. The earlier arrived waveform will tend to fall in the late systole and superimposes on the forward wave, thereby increasing AP and C-PP (*22*, *23*). By employing the AP and C-PP as indices of aortic stiffness, we were able to show that ISH and SDH patients had significantly higher aortic stiffness than the IDH and normotensive patients, which was consistent with the comparison using brachial PP as the index of aortic stiffness. It should be noted that another central pressure parameter, AIx, was not significantly different among the four hypertension subtypes. This might have been due to the masking effect of AIx calculation. Our previous work showed that AP and C-PP usually increased simultaneously when the aorta became stiffer, while AP and C-PP were used as the numerator and denominator in the formula used to calculate AIx (*24*). Therefore, there appears to be a mathematical flaw in the formula for calculating AIx, with the result that the changes in aortic stiffness are not reflected sensitively by AIx. On the other hand, although central pressure parameters are theoretically ideal indices of aortic stiffness, they are generated by a mathematic transfer function rather than actually being measured in an invasive fashion. Given the criticism of this mathematical transfer function in the literature (*25*, *26*), it seems not appropriate to consider these central parameters as ideal indices of aortic stiffness. To validate the above results, we further introduced carotid-femoral PWV as a true marker of aortic stiffness. PWV is recommended as one of the best methods for measuring aortic stiffness (*20*, *27*) and is the measure used in most large clinical studies (*28*–*30*). Our study showed repeatedly that PWV was highest in the ISH group, followed by the SDH, normotension and IDH groups, although the difference in PWV between the IDH and normotension groups was not significant (Fig. 1). Therefore, the present study clearly demonstrated the difference in aortic stiffness among the different hypertension subtypes, since brachial PP, central pressure parameters and PWV were all employed as indices to assess aortic stiffness.

Power of Reproducibility in the Present Study

In the present study, IDH accounted for about 8% of all study patients, which was very similar to the reported range of 6%–9% for this subtype in the National Health Examination Survey (NHES) (*31*) and National Health and Nutrition Examination Survey (NHANES) (*32*). We also found that the mean age in the IDH subtype group was 48±14 years, which was significantly younger than the mean ages in the ISH and normotension subtype groups (Table 2), a result very similar to previous studies addressing the prognostic value of IDH and other hypertension subtypes (*7*–*10*). This result was also consistent with a previous conclusion that IDH was the most frequent form of hypertension in young adults (*2*). However, this discrepancy in age among the different hypertension subtypes limited our ability to draw definitive conclusions, since age is a well-known factor influencing aortic stiffness (*33*). Therefore, the finding that aortic stiffness differed among hypertension subtypes could not be accepted as definitive, despite the fact that brachial PP and central pressure parameters indicated such a variation. To overcome this intrinsic discrepancy in age and other confounding factors, such as diabetic status, gender, dialysis duration and antihypertensive medication, a covariate analysis was performed, in which all these confounding factors were treated as covariates. The results showed that the differences in carotid-femoral PWV among the four groups were still significant (Fig. 1). Therefore, it was reasonable to conclude that the difference in aortic stiffness among the different hypertension subtypes was not affected by the intrinsic discrepancy in age and other possible confounding factors.

Isolated Diastolic Hypertension: An Independent Subtype of Hypertension

Although IDH has been recognized for a long time, there is still some skepticism about its status as an independent subtype of hypertension (*34*). The opponents claim that IDH might be derived from a misclassification of normotension or ISH, since an overestimation of DBP or underestimation of SBP by the auscultation method cannot be completely ruled out (*34*). We agree that this situation is possible in some patients receiving office BP measurements. However, a study in Japan that classified hypertension subtypes by averaging several home BP measurements was still able to show that IDH was associated with better prognosis (*9*). Specifically, the IDH patients had a lower risk of cardiovascular mortality than the normotensive patients in that study (*9*). If IDH was really generated by a misclassification of normotension, it seems unlikely that such a difference in cardiovascular risk would be seen between IDH and normotension. Furthermore, a recent report by the Framingham group found that the possibility of IDH transforming into SDH was significantly different from the possibility of normotension developing into SDH (*35*). In summary, these studies showed clearly that IDH was an independent subtype of hypertension in clinics.

It should be noted that certain indices of fluid status, such as the cardiac and thoracic ratio (CTR), Vena Cava diameter or atrial natriuretic peptide levels, would have contributed greatly to the present analysis, had they been available, since fluid overload is widely recognized to play an important role in the pathogenesis of hypertension in dialysis patients (*36*). A previous study has shown that fluid overload is very common in dialysis patients (*36*), and hypertensive dialysis patients usually have more extracellular water than normotensive dialysis patients (*37*). Whether fluid status also has some effect on aortic stiffness is not clear at present, but we believe that the availability of these indices would help us to understand more, if not all, about the underlying mechanism of the present findings. A future study employing such measurements of fluid status is warranted to address this important issue.

Limitations of the Present Study

This study had some limitations. First, it was a cross-sectional study, which prevented us from drawing any definitive conclusions regarding causality. Second, it was performed in a relatively elderly population (the mean age was 60 years), which meant that the sample in the IDH group was especially small, because this type of hypertension is mainly observed in young subjects. There is thus need of a future study employing young subjects to validate our results. Third, the percentage of patients under antihypertensive medication was high (range: 61 to 81%), which was fairly typical in dialysis patients. Although this percentage in the normotensive and IDH groups was lower than that in the ISH and SDH groups, it was still possible that different antihypertensive categories or doses in different hypertension subtypes might have affected the assessment of aortic stiffness. A future study performed in untreated subjects could overcome this limitation, although such an investigation would be difficult. Finally, the classification of hypertension subtypes was based on office BP measurements. Although much effort was made to minimize the influence of the white-coat effect and circadian variation in BP, we believe that 24-h ambulatory BP monitoring would provide better information for BP classification.

In conclusion, this cross-sectional study performed in CAPD patients showed that the aortic stiffness was significantly different among different hypertension subtypes: ISH and SDH patients had higher aortic stiffness than normotensive and IDH patients. The aortic stiffness in the ISH group was also higher than that in the SDH group, while there was no significant difference in aortic stiffness between the normotension and IDH groups. This result may help to clarify the power of hypertension subtypes to predict cardiovascular mortality.

Acknowledgements

We are sincerely grateful to all the nurses in the Peritoneal Dialysis Center, Peking University Third Hospital.

References

1. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA* 2003; **289**: 2560–2572.
2. Franklin SS, Jacobs MJ, Wong ND, L'Italien GJ, Lapuerta P: Predominance of isolated systolic hypertension among middle-aged and elderly US hypertensives: analysis based on National Health and Nutrition Examination Survey (NHANES) III. *Hypertension* 2001; **37**: 869–874.
3. Burt VL, Whelton P, Roccella EJ, *et al*: Prevalence of hypertension in the US adult population. Results from the Third National Health and Nutrition Examination Survey, 1988–1991. *Hypertension* 1995; **25**: 305–313.
4. Kannel WB, Dawber TR, McGee DL: Perspectives on systolic hypertension. The Framingham study. *Circulation*

1980; **61**: 1179–1182.
5. Liu L, Wang JG, Gong L, Liu G, Staessen JA: Comparison of active treatment and placebo in older Chinese patients with isolated systolic hypertension. Systolic Hypertension in China (Syst-China) Collaborative Group. *J Hypertens* 1998; **16**: 1823–1829.
6. Staessen JA, Fagard R, Thijs L, *et al*: Randomised double-blind comparison of placebo and active treatment for older patients with isolated systolic hypertension. The Systolic Hypertension in Europe (Syst-Eur) Trial Investigators. *Lancet* 1997; **350**: 757–764.
7. Fang J, Madhavan S, Cohen H, Alderman MH: Isolated diastolic hypertension. A favorable finding among young and middle-aged hypertensive subjects. *Hypertension* 1995; **26**: 377–382.
8. Petrovitch H, Curb JD, Bloom-Marcus E: Isolated systolic hypertension and risk of stroke in Japanese-American men. *Stroke* 1995; **26**: 25–29.
9. Hozawa A, Ohkubo T, Nagai K, *et al*: Prognosis of isolated systolic and isolated diastolic hypertension as assessed by self-measurement of blood pressure at home: the Ohasama study. *Arch Intern Med* 2000; **160**: 3301–3306.
10. Strandberg TE, Salomaa VV, Vanhanen HT, Pitkala K, Miettinen TA: Isolated diastolic hypertension, pulse pressure, and mean arterial pressure as predictors of mortality during a follow-up of up to 32 years. *J Hypertens* 2002; **20**: 399–404.
11. Muntinga JH, Heesen WF, Smit AJ, Visser KR, May JF: Isolated systolic hypertension from a vascular point of view. *J Vasc Res* 2000; **37**: 485–493.
12. O'Rourke MF, Nichols WW: Aortic diameter, aortic stiffness, and wave reflection increase with age and isolated systolic hypertension. *Hypertension* 2005; **45**: 652–658.
13. Ni Y, Wang H, Hu D, Zhang W: The relationship between pulse wave velocity and pulse pressure in Chinese patients with essential hypertension. *Hypertens Res* 2003; **26**: 871–874.
14. Pickering TG: Isolated diastolic hypertension. *J Clin Hypertens* 2003; **5**: 411–413.
15. Chen CH, Ting CT, Nussbacher A, *et al*: Validation of carotid artery tonometry as a means of estimating augmentation index of ascending aortic pressure. *Hypertension* 1996; **27**: 168–175.
16. Chen CH, Nevo E, Fetics B, *et al*: Estimation of central aortic pressure waveform by mathematical transformation of radial tonometry pressure. Validation of generalized transfer function. *Circulation* 1997; **95**: 1827–1836.
17. Asmar R, Benetos A, Topouchian J, *et al*: Assessment of arterial distensibility by automatic pulse wave velocity measurement: validation and clinical application study. *Hypertension* 1995; **26**: 485–490.
18. Tanaka M, Babazono T, Takeda M, Iwamoto Y: Pulse pressure and chronic kidney disease in patients with type 2 diabetes. *Hypertens Res* 2006; **29**: 345–352.
19. Miyagi T, Muratani H, Kimura Y, *et al*: Increase in pulse pressure relates to diabetes mellitus and low HDL cholesterol, but not to hyperlipidemia in hypertensive patients aged 50 years or older. *Hypertens Res* 2002; **25**: 335–341.
20. O'Rourke MF, Staessen JA, Vlachojannis JA, Duprez D, Plante GE: Clinical application of arterial stiffness: definitions and reference values. *Am J Hypertens* 2002; **15**: 426–444.
21. Van Bortel LM, Duprez D, Starmans-Kool MJ, *et al*: Clinical applications of arterial stiffness, Task Force III: recommendations for user procedures. *Am J Hypertens* 2002; **15**: 445–452.
22. Kelly R, Hayward C, Avolio A, O'Rourke M: Noninvasive determination of age-related changes in the human arterial pulse. *Circulation* 1989; **80**: 1652–1659.
23. O'Rourke MF, Mancia G: Arterial stiffness. *J Hypertens* 1999; **17**: 1–4.
24. Cheng LT, Tang LJ, Cheng L, Huang HY, Wang T: Limitation of the augmentation index for evaluating arterial stiffness. *Hypertens Res* 2007; **30**: 713–722.
25. Millasseau SC, Patel SJ, Redwood SR, Ritter JM, Chowienczyk PJ: Pressure wave reflection assessed from the peripheral pulse: is a transfer function necessary? *Hypertension* 2003; **41**: 1016–1020.
26. Davies JI, Struthers AD: Pulse wave analysis and pulse wave velocity: a critical review of their strengths and weaknesses. *J Hypertens* 2003; **21**: 463–472.
27. Pannier BM, Avolio AP, Hoeks A, Mancia G, Takazawa K: Methods and devices for measuring arterial compliance in humans. *Am J Hypertens* 2002; **15**: 743–753.
28. Blacher J, Guerin AP, Pannier B, Marchais SJ, Safar ME, London GM: Impact of aortic stiffness on survival in end-stage renal disease. *Circulation* 1999; **99**: 2434–2439.
29. Laurent S, Boutouyrie P, Asmar R, *et al*: Aortic stiffness is an independent risk predictor of all-cause and mortality in hypertensive patients. *Hypertension* 2001; **37**: 1236–1241.
30. Boutouyrie P, Tropeano AI, Asmar R, *et al*: Aortic stiffness is an independent predictor of primary coronary events in hypertensive patients: a longitudinal study. *Hypertension* 2002; **39**: 2085–2090.
31. Gordon G: Blood Pressure of Adults by Age and Sex, United States, 1960–62. National Center for Health Statistics, Series II, No. 4. Washington DC, 1964.
32. Drizd T, Dannenberg AL, Engel A: Blood pressure levels in persons 18–74 years of age in 1976–80, and trends in blood pressure from 1960 to 1980 in the United States. *Vital Health Stat* 1986; **11**: 1–68.
33. Sasaki R, Yamano S, Yamamoto Y, *et al*: Vascular remodeling of the carotid artery in patients with untreated essential hypertension increases with age. *Hypertens Res* 2002; **25**: 373–379.
34. Blank SG, Mann SJ, James GD, West JE, Pickering TG: Isolated elevation of diastolic blood pressure. Real or artifactual? *Hypertension* 1995; **26**: 383–389.
35. Franklin SS, Pio JR, Wong ND, *et al*: Predictors of new-onset diastolic and systolic hypertension: the Framingham Heart Study. *Circulation* 2005; **111**: 1121–1127.
36. Enia G, Mallamaci F, Benedetto FA, *et al*: Long-term CAPD patients are volume expanded and display more severe left ventricular hypertrophy than haemodialysis patients. *Nephrol Dial Transplant* 2001; **16**: 1459–1464.
37. Katzarski KS, Charra B, Luik AJ, *et al*: Fluid state and blood pressure control in patients treated with long and short haemodialysis. *Nephrol Dial Transplant* 1999; **14**: 369–375.